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Clinical-pathologic correlation of association and reciprocity of biliary and gastrointestinal tract disease with acute pancreatitis

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A CLINICAL-PATHOLOGIC CORRELATION OF ASSOCIATION AND RECIPROCITY OF BILIARY AND GASTROINTESTINAL TRACT DISEASE WITH ACUTE PANCREATITIS

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INTRODUCTION AND HISTORY

The first recorded anatomical description of the pancreas was by Ruphas or Rufus of Ephesus in 100 A. D. Reiner de Graaf (1641-1673) published his thesis in 1664 describing cannulation of the pancreatic duct, the bile duct, and the parotid duct in the dog and his somewhat misguided understanding of functions and various properties of pancreatic juice. Claude Bernard (1813-1878) also studied the action of pancreatic enzymes on proteins, carbohydrates and fats from 1849 to 1856. He obtained diabetes mellitus in the dog by puncturing the fourth ventricle in 1849 and found hyperglycemia and glycosuria in diabetes in 1858.[6, 10, 22]

Occurence of fatal diabetes postpancreatectomy in the dog was described in 1890 by J. Von Mering and O. Minkowski and later, in 1892, the ability of autogenous grafts of pancreatic tissue to prevent the fatal outcome. They also showed removal of the grafts allowed the fatal course of the disease to continue.[22] The myriad efforts of early researchers lead to the success of F. G. Banting and C. H. Best in 1922 when they isolated insulin and their associate, J. B. Collip, standardized the material for clinical purposes. Searle Harris in 1923 and later many others investigated the properties of the newly available hormone and soon there were descriptions of a possible spontaneous hyperinsulinism syndrome and its confirmation.[22]

The first clear pathologic and diagnostic description of acute pancreatitis was made by the Boston pathologist, Reginald

Fitz, in 1889, according to A. O. Whipple.[22] The disease entity of chronic pancreatitis seems to have been first defined in 1842 by H. J. Claessen.[6, 10] Apparantly H. H. Spiers was the first to describe a case of acute hemorrhagic pancreatitis.[6] In 1878, N. Friedreich differentiated primary and secondary chronic interstitial pancreatitis and was familiar with the writings of Claessen (1842) and Ancelet (1866) and also of J. Klob from 1860 wherein Klob described the chalky areas and hemorrhage seen in the fibrotic pancreas. Two types of pancreatitis were described by L. Oser in 1898.[6, 10] Oser's first type involved the entire gland and resulted from toxic agents entering through the vascular and lymphatic channels and also through the ducts and he considered alcoholism and biliary disease to be etiologic mechanisms. Oser's second type was a so-called circumscribed pancreatitis resulting from penetrating lesions from the adjacent duodenum and stomach.[6, 10, 22]

When Opie published his report in 1901 and propounded his "common channel" theory he precipitated a great deal of research, both pro and con, which even today has not settled this question to the satisfaction of all.[6, 10, 16, 22] Although the anatomical situation described by Opie exists in only approximately 15 per cent of the population the struggle goes on, and many papers seem initiated for no other purpose than to throw themselves anew into the fray, in spite of an abundance of evidence on both sides.[6, 10, 16, 20, 22, 36, 49, 51]

The myriad difficulties in diagnosing pancreatitis, both acute and chronic, are well documented and the criteria of greatest importance recorded by one author may well be listed as being of little significance by another.[6, 9, 10, 12, 16-18, 26, 32, 33, 40, 43-45, 52] There is also considerable disagreement as to the most common or the primary etiologic agents. This is usually most noticeable where an author has accumulated several different studies on any one etiologic mechanism, i.e., the function of alcoholism as the primary cause for chronic pancreatitis is sure to get strong reactions pro and con. Collected series show a great variance from around 10.0 to as high as 100 per cent for the alcoholic etiology being the primary cause.[6, 22]

The etiologies of pancreatitis are classified into broad categories with various subgroups by Blumenthal and Probstein.[6] Howard lists the rigid categories of, "(1) alcoholism, (2) gallstones, (3) parathyroid adenoma, (4) familial hyperlipemia, (5) ampullary carcinoma, (6) idiopathic, and (7) postoperative pancreatitis."[22] However, other etiologies are abundant in the literature, thereby arguing for the more flexible classification, and range from sulfamethizole,[3] the diuretic chlorthalidone,[24] abdominal trauma in a child,[4] pancreatic antibodies or autoimmune mechanism,[13, 28, 29] incomplete pancreatic duct obstruction,[20] the role of the parathyroid glands in calcium and magnesium metabolism in acute hemorrhagic pancreatitis,[21] Selye's recent

experimental production of cholangitis and pancreatitis by ferric oxide saccharate,[42] chronic alcoholism,[34] reciprocal association with liver disease,[9, 44] and the role of bile reflux in pancreatitis.[51]

The studies of Gajdusek and Larkin in 1958,[15] Thal et al.,[46] and Fonkalsrud and Longmire in 1961[13] have demonstrated circulating antibodies to pancreatic tissue in patients with chronic pancreatitis, and in some the apparant existence of multiple antibodies.[13] Thal et al. have made clinical applications and found specific pancreatic antibodies where the common pathology was chronic destruction of pancreatic acinar tissue, noting some false positive reactions in patients with widespread carcinomatosis.[46]

The reciprocal association of pancreatitis with liver disease, diabetes mellitus, and gastrointestinal tract lesions is of considerable interest. Although one group made a great effort to study pancreatitis patients having no history or any indications of biliary or gastrointestinal tract disease they found upon autopsy and surgical investigation these patients had significant amounts of reciprocal pathology.[9] Steigman and Chung stress the receprocity between liver and pancreatic disease quite heavily.[44] The work of other authors demonstrates the existence of such a relationship, either separately or collectively, when they are reviewed.[6, 8, 9, 11, 14, 22, 26, 27, 47, 49, 51]

The knowledge that there is a tendency toward reciprocity of disease between the pancreas and the surrounding organs can be valuable in certain patients and cognizance of this trend may on occasion enable us to institute a more vigorous program of diagnosis and broader base of therapy. Since many authors, as indicated above, have described pancreatitis as one of the most often missed or misdiagnosed of disease entities it would seem anything that brings pancreatitis to our attention and causes us to appropriately rule it out or in would be of value. Such an attempt will be made with regard to the pancreas, the biliary system, and the gastrointestinal tract. There will be no efforts to describe the multiple symptoms and complaints or the physical findings on admission.

MATERIALS AND METHODS

The data for this study were obtained from the autopsy files and the medical records of the Pathology Department and of the Medical Records Department of the Bishop Clarkson Memorial Hospital. The patients studied were those who were listed in the autopsy files as having acute pancreatitis as the cause of death and those who died of other causes, but acute pancreatitis was present as an incidental or contributory finding. This report covers the years 1950 through 1963. A comparison of the data in the present series with the literature is made.

RESULTS

There was a total of twenty-five patients, with an almost equal sex distribution consisting of thirteen women and twelve men. Table I, page 7, lists the distribution of the patients by their age and sex group. None of the patients fell into any of the age groups below forty years nor were there any older than eighty-eight years. Women in the 40 to 49 year group made up 24 per cent of the total deaths, while men in this age group comprised only 4 per cent of the total deaths. The highest per cent of deaths for the group of men was in the 60 to 69 year group at which time they comprised 28.0 per cent of the group total as against 12.0 per cent for the women. Of the total group five were listed as deaths resulting from pancreatitis, two females ages 44 and 49 years, and three males ages 60, 62, and 65. Additionaly,

TABLE I

AGE AND SEX DISTRIBUTION OF PATIENTS

AGE GROUP	AGE AND SEX	% OF TOTAL PATIENTS	% OF SEX GROUP
40-49	40-F, 44-F, 47-F, 48-F, 49-F 47-F	24.0	46.2
	40-M	4.0	8.3
50-59	51-M	4.0	8.3
60-69	60-F, 64-F, 68-F	12.0	23.1
	60-M, 62-M, 65-M, 66-M, 67-M, 69-M 62-M	28.0	58.4
70-79	77-F	4.0	7.7
	71-M, 73-M, 79-M	12.0	25.0
80-89	84-F, 86-F, 88-F	12.0	23.1

(F = Female, M = Male)

pancreatitis may have been a significant contributing factor in the death of one other patient, a 64 year old woman.

Table II, on pages 8 and 9, sets forth the various types of pathology found in the liver and biliary system. Fatty metamorphosis in three females and five males totaling 32 per cent of all patients. Congestion of the liver was present in nineteen patients or 76 per cent. Ascites was present in ten patients or 40 per cent. Cholangitis was found in three patients, 12 per cent, and in one, a 60 year old man, was listed as being secondary to his acute pancreatitis. The incidence of cholelithiasis was 28 per cent, four women and three men. Cholecystitis was

TABLE II

PATHOLOGY IN LIVER AND BILIARY SYSTEM

PATHOLOGY	GROUP 40 - 49		GROUP 50 - 59		GROUP 60 - 69		GROUP 70 - 79		GROUP 80 - 89	
	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Fatty Metamorphosis	3-F	12.0	- -	- -	- -	- -	- -	- -	- -	- -
	1-M	4.0	1-M	4.0	3-M	12.0	- -	- -	- -	- -
Congestion of Liver	3-F	12.0	- -	- -	3-F	12.0	1-F	4.0	3-F	12.0
	1-M	4.0	1-M	4.0	5-M	20.0	2-M	8.0	- -	- -
Ascites	2-F	8.0	- -	- -	1-F	4.0	1-F	4.0	- -	- -
	- -	- -	- -	- -	4-M	16.0	2-M	8.0	- -	- -
Cholangitis	- -	- -	- -	- -	1-F	4.0	- -	- -	- -	- -
	- -	- -	- -	- -	2-M	8.0	- -	- -	- -	- -
Cholelithiasis	1-F	4.0	- -	- -	2-F	8.0	- -	- -	1-F	4.0
	- -	- -	- -	- -	1-M	4.0	- -	- -	- -	- -
Cholecystitis	- -	- -	- -	- -	1-F	4.0	- -	- -	1-F	4.0
	- -	- -	- -	- -	1-M	4.0	1-M	4.0	- -	- -
Hepatitis	2-F	8.0	- -	- -	- -	- -	- -	- -	- -	- -
	- -	- -	- -	- -	- -	- -	- -	- -	- -	- -
Jaundice	3-F	12.0	- -	- -	1-F	4.0	1-F	4.0	- -	- -
	- -	- -	1-M	4.0	3-M	12.0	- -	- -	- -	- -
Metastases in Liver	1-F	4.0	- -	- -	- -	- -	- -	- -	1-F	4.0
	- -	- -	- -	- -	- -	- -	- -	- -	- -	- -
Hepatomegaly	4-F	16.0	- -	- -	- -	- -	- -	- -	- -	- -
	- -	- -	1-M	4.0	3-M	12.0	1-M	4.0	- -	- -
History of Alcoholism	2-F	8.0	- -	- -	- -	- -	- -	- -	- -	- -
	- -	- -	- -	- -	- -	- -	- -	- -	- -	- -
Gallbladder Surg. Absent	- -	- -	- -	- -	1-F	4.0	- -	- -	2-F	8.0
	- -	- -	- -	- -	1-M	4.0	- -	- -	- -	- -
Gallbladder Distended	1-F	4.0	- -	- -	1-F	4.0	- -	- -	- -	- -
	- -	- -	- -	- -	- -	- -	1-M	4.0	- -	- -

TABLE II (CONTINUED)

PATHOLOGY IN LIVER AND BILIARY SYSTEM

PATHOLOGY	GROUP 40-49		GROUP 50-59		GROUP 60-69		GROUP 70-79		GROUP 80-89	
	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Cirrhosis (all types)	3-F	12.0	- -	- -	1-F	4.0	- -	- -	- -	- -
	- -	- -	- -	- -	3-M	12.0	2-M	8.0	- -	- -
Fatty Nutritional Cirrh.	1-F	4.0	- -	- -	- -	- -	- -	- -	- -	- -
	- -	- -	- -	- -	1-M	4.0	2-M	8.0	- -	- -
Biliary Cirrhosis	1-F	4.0	- -	- -	1-F	4.0	- -	- -	- -	- -
	- -	- -	- -	- -	1-M	4.0	- -	- -	- -	- -
Post-necrotic Cirrhosis	1-F	4.0	- -	- -	- -	- -	- -	- -	- -	- -
	- -	- -	- -	- -	1-M	4.0	- -	- -	- -	- -
Bile Stasis	- -	- -	- -	- -	1-M	4.0	- -	- -	- -	- -
Retention cyst of Liver	- -	- -	- -	- -	1-M	4.0	- -	- -	- -	- -
Hemangioma of Liver	- -	- -	- -	- -	1-M	4.0	- -	- -	- -	- -
Thrombotic Thrombocytopenic Purpura of Liver	1-F	4.0	- -	- -	- -	- -	- -	- -	- -	- -

(F = Female, M = Male)

found in two females, both chronic, and two males, one with chronic and the other with subacute and chronic, for a total of 16 per cent. Hepatitis in two women, aged 40 and 47, and was listed as slight or low grade. Jaundice was present in nine patients, or 36 per cent, and varied from slight, with serum bilirubin of 5.1 mg/100 ml., to marked with bilirubin levels of 28.0 to 31.2 mg/100 ml. Metastatic carcinoma was present in two female patients, ages

49 and 84, and in both was adenocarcinoma from the intestinal tract. The gallbladder was surgically absent in four patients, 16 per cent, one 64 year old female being in her eleventh post-operative day and a 67 year old male had his cholecystectomy approximately 6 to 7 weeks prior to his death at an Air Force Hospital in California and suffered an ingravescent post-operative course prior to his admission at Clarkson Hospital.

A recorded history of alcoholism was obtained in only two of these patients, a total of 8.0 per cent. One of the women, a 40 year old, was listed as having chronic leptomeningitis consistent with chronic alcoholism and there was early degeneration of the brain. This woman also had a slight acute hepatitis and an acute hemorrhagic pancreatitis. She had boarded a train for Omaha and after a five hour ride was found in the ladies lounge, when the train arrived in Omaha, apparantly in poor condition. She was dead on arrival at the hospital. The alcohol level of the blood was 0.05%, the urine 0.2%, and the cerebrospinal fluid 0.2%, levels not usually associated with fatalities. The other patient, a woman aged 47 years, had a history of alcoholism, daily intake not determined, Laennec's cirrhosis, an ascites of 3,000 cc., hepatomegaly(weight not recorded), and a bilirubin of 31.2 mg/100 ml. This 47 year old woman had both acute and chronic pancreatitis at autopsy.

Hepatomegaly was assigned these patients with a liver which

weighed in excess of 2,000 grams. Morris' Human Anatomy, 11th edition, 1953, lists the size range as 1,000 to 2,000 grams with average as 1,500 grams and states there are many factors in assigning hepatomegaly to any one patient. While it is realized such classification could be in error there were no instances where such assignment was contrary to that of the prosector. Three patients were found to have livers in the lower range. All were women, the first aged 64 had a 950 gram liver, the second aged 77 had a 1,100 gram liver, and the third aged 88 had a 1,000 gram liver.

Cirrhosis of the liver, all types, totaled nine patients or 36 per cent, four women and five men. Three types of cirrhosis were found, (1) fatty nutritional, four patients or 16 per cent, (2) biliary, three patients, 12 per cent, and (3) post-necrotic, two patients or 8 per cent. Only one of these patients had a history of alcoholism recorded, the 47 year old woman described previously.

Bile stasis was found in one patient only, a 62 year old male, who had been admitted to another hospital where a diagnosis of acute pancreatitis had been made. The day after his admission he had a cholecystostomy performed with removal of gallstones. Following his operation he became oliguric and then uremic with an ingravescent course. He was transferred from the other hospital to the Bishop Clarkson Hospital on his fifth post-operative day for hemodialysis on the artificial kidney. In spite of two

sessions of hemodialysis and other vigorous therapeutic measures, the patient continued on his downhill course and expired as a result of his hemorrhagic pancreatitis and gastrointestinal hemorrhage. No extrahepatic biliary obstruction was found.

A 69 year old male was found to have both a retention cyst of the liver, 15 mm. in greatest diameter, containing clear fluid and a hemangioma.

One instance of thrombotic thrombocytopenic purpura was found in a 47 year old female with involvement of not only liver and pancreas, but also heart, lungs, adrenals, kidneys and skin. There was no mention of the gastrointestinal tract in her autopsy report. Her autopsy report stated the immediate cause of death could not be demonstrated on either the gross or microscopic findings due to the brain being inadvertently discarded.

Table III, page 13, lists the pathology found in these patients with regard to the pancreas. Death due to pancreatitis occurred in five of these patients and questionably in a sixth. Six of the twenty-five, 24 per cent, were found to have evidence of chronic pancreatitis. Three other patients in addition to these six were found to have calcium deposits in the pancreas. There was no apparant fibrosis or fat infiltration of the pancreas listed for two of these three patients, but both of these lesions were present in the third patient. Two of these patients with calcium deposits in the pancreas had fat necrosis

TABLE III

PATHOLOGY IN THE PANCREAS

PATHOLOGY	GROUP 40-49		GROUP 50-59		GROUP 60-69		GROUP 70-79		GROUP 80-80	
	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Acute Pancreatitis	6-F 1-M	24.0 4.0	- - 1-M	- - 4.0	3-F 7-M	12.0 28.0	1-F 3-M	4.0 12.0	3-F - -	12.0 - -
Chronic Pancreatitis	3-F - -	12.0 - -	- - - -	- - - -	1-F - -	4.0 - -	1-F 1-M	4.0 4.0	- - - -	- - - -
Hemorrhagic Pancreatitis	1-F - -	4.0 - -	- - - -	- - - -	- - 3-M	- - 12.0	- - - -	- - - -	- - - -	- - - -
Necrotizing Pancreatitis	2-F - -	8.0 - -	- - - -	- - - -	- - 3-M	- - 12.0	- - - -	- - - -	- - - -	- - - -
Fat Infiltration of Panc.	1-F - -	4.0 - -	- - - -	- - - -	1-F 3-M	4.0 12.0	1-F 1-M	4.0 4.0	3-F - -	12.0 - -
Fat Necrosis	4-F - -	16.0 - -	- - - -	- - - -	1-F 5-M	4.0 20.0	1-F - -	4.0 - -	- - - -	- - - -
Fibrosis of Pancreas	2-F - -	8.0 - -	- - - -	- - - -	- - - -	- - - -	1-F 2-M	4.0 8.0	2-F - -	8.0 - -
Calcium Deposits in Panc.	1-F - -	4.0 - -	- - - -	- - - -	- - 3-M	- - 12.0	1-F - -	4.0 - -	- - - -	- - - -
Edema of Pancreas	2-F - -	8.0 - -	- - 1-M	- - 4.0	1-F 3-M	4.0 12.0	- - - -	- - - -	- - - -	- - - -
Diabetes Mellitus*	- - - -	- - - -	- - - -	- - - -	- - 1-M	- - 4.0	- - 1-M	- - 4.0	- - - -	- - - -
Islet Cell Changes	1-F - -	4.0 - -	- - 1-M	- - 4.0	2-F 1-M	8.0 4.0	- - - -	- - - -	1-F - -	4.0 - -

(F = Female, M = Male)

*Two additional patients had hyperglycemia, a 44 year old female and a 68 year old female.

in the organ. The deposition of large amounts of calcium in areas of fat necrosis in acute pancreatitis, which may in some instances equal or exceed the total "circulating" calcium, has been noted by other authors, who advocate the administration of calcium to combat this depletion.[6, 22, 52] The total with calcium depostion was five, or 20 per cent.

A hemorrhagic type pancreatitis was present in four of the patients, 16 per cent. A necrotizing pancreatitis was found in 20 per cent. Edema of the pancreas was noted in 28 per cent. Fat infiltration of the pancreas was present in 40 per cent. Fat necrosis was found in 44 per cent.

Diabetes mellitus is known to be a complication in some instances of pancreatitis, both acute and chronic. Both the 65 year old male and the 71 year old male were known diabetics. The 65 year old patient entered the hospital with a blood sugar of 776 mg/100 ml. The 71 year old had been on a daily dosage schedule of 60 units of protamine zinc insulin for several years. The islet cells of the 65 year old showed a moderate amount of hyalinization. Two female patients, ages 44 and 68 years, had hyperglycemia, but no history of diabetes. It is thought that their hyperglycemia could be due either to a previously undiagnosed diabetes mellitus or as a result of the pancreatitis, since the islet cells of the 44 year old were enlarged and granular and those of the 68 year old showed some necrosis.

TABLE IV

PATHOLOGIC CONDITIONS OF THE GASTROINTESTINAL TRACT

SURGICAL PROCEDURES	GROUP 40-49 NO.	%	GROUP 50-59 NO.	%	GROUP 60-69 NO.	%	GROUP 70-79 NO.	%	GROUP 80-89 NO.	%
For Disease of G-I Tract	3-F	12.0	- -	- -	2-F	8.0	- -	- -	2-F	8.0
	- -	- -	- -	- -	5-M	20.0	- -	- -	- -	- -
Abdom. Ops. for Other Organ Sys.	3-F	12.0	- -	- -	- -	- -	- -	- -	- -	- -
	- -	- -	- -	- -	2-M	8.0	1-M	4.0	- -	- -
ESOPHAGUS										
Esophageal Varices	1-F	4.0	- -	- -	- -	- -	- -	- -	- -	- -
	- -	- -	- -	- -	1-M	4.0	1-M	4.0	- -	- -
Esophageal Perforation	- -	- -	- -	- -	1-F	4.0	- -	- -	- -	- -
	- -	- -	- -	- -	1-M	4.0	- -	- -	- -	- -
Esophagitis	- -	- -	- -	- -	2-M	8.0	- -	- -	- -	- -
Esophagectomy	- -	- -	- -	- -	1-M	4.0	- -	- -	- -	- -
STOMACH										
Ulcers	- -	- -	1-M	4.0	1-M	4.0	- -	- -	- -	- -
Hemorrhage	1-F	4.0	- -	- -	1-F	4.0	- -	- -	1-F	4.0
	- -	- -	1-M	4.0	2-M	8.0	- -	- -	- -	- -
Chronic Gastritis	- -	- -	- -	- -	- -	- -	- -	- -	1-F	4.0
Polypoid Adeno-carcinoma	- -	- -	- -	- -	- -	- -	- -	- -	1-F	4.0
Leiomyoma	- -	- -	- -	- -	1-M	4.0	- -	- -	- -	- -
Infarct	- -	- -	- -	- -	1-M	4.0	- -	- -	- -	- -
Partial Obstruction	- -	- -	- -	- -	- -	- -	- -	- -	1-F	4.0
Gastroenteritis	- -	- -	1-M	4.0	1-M	4.0	- -	- -	- -	- -

TABLE IV (CONTINUED)

PATHOLOGIC CONDITIONS OF THE GASTROINTESTINAL TRACT

STOMACH (Continued)	GROUP 40-49		GROUP 50-59		GROUP 60-69		GROUP 70-79		GROUP 80-89	
	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Subtotal Gastrectomy with Gastrojejunostomy	- -	- -	- -	- -	1-F 2-M	4.0 8.0	- -	- -	- -	- -
Subtotal Gastrectomy, cardiac portion	- -	- -	- -	- -	1-M	4.0	- -	- -	- -	- -
Gastrostomy	- -	- -	- -	- -	1-M	4.0	- -	- -	- -	- -
Gastrojejunostomy Separation	- -	- -	- -	- -	1-M	4.0	- -	- -	- -	- -
Marked Dilatation	- -	- -	- -	- -	1-M	4.0	- -	- -	- -	- -
Submucosal Lipid Placques, distal stomach	- -	- -	- -	- -	- -	- -	- -	- -	1-F	4.0
SMALL INTESTINE										
Passive Congestion	- -	- -	- -	- -	- -	- -	1-M	4.0	- -	- -
Infarct	- -	- -	- -	- -	- -	- -	- -	- -	1-F	4.0
Lumen filled with old clotted blood	- -	- -	1-M	4.0	- -	- -	- -	- -	- -	- -
Focal submucosal Hemorrhage or Petechiae	- -	- -	- -	- -	1-F 1-M	4.0 4.0	- -	- -	- -	- -
DUODENUM										
Focal ulceration of Pylorus	- -	- -	- -	- -	1-M	4.0	- -	- -	- -	- -
Ulcer penetrating into Pancreas	- -	- -	- -	- -	1-M	4.0	- -	- -	- -	- -

TABLE IV (CONTINUED)

PATHOLOGIC CONDITIONS OF THE GASTROINTESTINAL TRACT

DUODENUM (Continued)	GROUP 40-49		GROUP 50-59		GROUP 60-69		GROUP 70-79		GROUP 80-89	
	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Pancreatic Enzyme Necrosis	1-F	4.0	- -	- -	- -	- -	- -	- -	- -	- -
JEJUNUM										
Jejunostomy	- -	- -	- -	- -	- -	- -	- -	- -	1-F	4.0
Pancreatic Enzyme Necrosis	1-F	4.0	- -	- -	- -	- -	- -	- -	- -	- -
ILEUM										
Infarct probably due to Volvulus	- -	- -	- -	- -	- -	- -	- -	- -	1-F	4.0
Hamartoma from Panc. in wall	- -	- -	- -	- -	- -	- -	- -	- -	1-F	4.0
Ileostomy	1-F	4.0	- -	- -	- -	- -	- -	- -	- -	- -
COLON										
Diverticulosis	- -	- -	- -	- -	1-F	4.0	- -	- -	1-F	4.0
	- -	- -	- -	- -	1-M	4.0	- -	- -	- -	- -
Colostomy	- -	- -	- -	- -	- -	- -	- -	- -	1-F	4.0
Necrosis	1-F	4.0	- -	- -	- -	- -	- -	- -	1-F	4.0
Partial Obstruction of Colostomy	- -	- -	- -	- -	- -	- -	- -	- -	1-F	4.0
Appendix	1-F	4.0	- -	- -	2-F	8.0	- -	- -	- -	- -
Surgically Absent	- -	- -	- -	- -	1-M	4.0	- -	- -	- -	- -
Recurrent Carcinoma in Colostomy	- -	- -	- -	- -	- -	- -	- -	- -	1-F	4.0
Adenocarcinoma of Rectum	- -	- -	- -	- -	- -	- -	1-M	4.0	- -	- -

TABLE IV (CONTINUED)

PATHOLOGIC CONDITIONS OF THE GASTROINTESTINAL TRACT

COLON (Continued)	GROUP 40-49 NO.	%	GROUP 50-59 NO.	%	GROUP 60-69 NO.	%	GROUP 70-79 NO.	%	GROUP 80-89 NO.	%
Submucosal Hemorrhage in Cecum and Rectum	1-F	4.0	- -	- -	- -	- -	- -	- -	- -	- -
Fibropurulent Colitis	- -	- -	- -	- -	1-M	4.0	- -	- -	- -	- -
Melena	1-F	4.0	- -	- -	1-F	4.0	- -	- -	- -	- -
	- -	- -	- -	- -	1-M	4.0	1-M	4.0	- -	- -
Peritonitis	1-F	4.0	- -	- -	- -	- -	- -	- -	2-F	8.0
	- -	- -	- -	- -	1-M	4.0	- -	- -	- -	- -

Table IV, pages 15 through 18, summarizes all the pathologic conditions found associated with the gastrointestinal tract. For the most part, the table is self-explanatory.

DISCUSSION

Table I, page 7, concerns the age and sex distribution of the patients in this series of acute pancreatitis. There was a total of 25 patients, 13 females and 12 males. There were no deaths due to or associated with acute pancreatitis in any patients who were younger than 40 years or older than 88 years. Blumenthal and Probstein studied a group of 163 autopsy patients and found acute pancreatitis present in the 0-10 year group 3.1 per cent for males and 0.6 per cent for females in their series. There was no occurrence in the 11-20 year olds and 0.6 per cent males and 1.8

per cent females in the 21-30 year olds. There were 7.4 per cent males and 2.9 per cent females in their 31-40 year olds. The following table compares the findings for the remaining age and sex groups for the two series.

TABLE V

AGE AND SEX DISTRIBUTION IN ACUTE PANCREATITIS

AGE GROUP	BLUMENTHAL & PROBSTEIN				CURRENT SERIES			
	MALE	PER CENT	FEMALE	PER CENT	MALE	PER CENT	FEMALE	PER CENT
31-40	7	4.3	2	1.2	1	4.0	1	4.0
41-50	15	9.2	12	7.4	0	0.0	5	20.0
51-60	16	9.8	8	4.9	2	8.0	1	4.0
61-70	28	17.2	20	12.3	6	24.0	2	8.0
71-80	20	12.3	17	10.4	3	12.0	1	4.0
81-Plus	2	1.2	6	3.7	0	0.0	3	12.0

It will be noted that in the age range 51-80 there is a much smaller per cent of female patients than found by Blumenthal and Probstein in their series. In the age ranges 31-40, 41-50, and 81-Plus the per cent of females in the current series is somewhat higher. In the age range 41-60 the per cent of males in the current series is markedly less, but increased in the 61-70 age range.

Liver and biliary system pathology and history of alcoholism are covered in Table II, pages 8 and 9. The question of alcohol in the etiology of acute and chronic pancreatitis is still a subject of controversy. In the current series a history of alco-

holism was obtained in only two patients, one of whom died as a result of alcoholism. The incidence of a history of alcoholism in the current series is 8 per cent. The reluctance of the patient and his family to have the label "chronic alcoholic" appear on his record is well known. There is considerable variation in incidence in the literature. Table VI, below, shows this variation in the literature as recorded by Blumenthal and Probstein.[6]

TABLE VI

ACUTE PANCREATITIS PATIENTS WITH ALCOHOLISM HISTORY

McWhorter	11.0%
Myers and Keefer	21.0%
Rich and Duff	29.0%
Weiner and Tennant	66.0%
Clark	18.0%
Paxton and Payne	18.0%
Bockus and Raffensberger	50.0%
Blumenthal and Probstein	3.5%*

(*6 out of 163 patients)

Howard and Jordan[22] record the incidence of alcoholism in acute pancreatitis as collected from 15 hospitals (7 charity, 1 veterans, and 7 general) covering 1,350 patients with 357 of them in the alcoholic class for an incidence of 26 per cent. Only 33 per cent of the 15 studies included autopsy material. The charity hospitals had the following percentages of alcoholism recorded, 34, 21, 39, 18, 22, 66, and 32 per cent for an average of 33.2 per cent. The veterans hospital reported 51 per cent. The general hospitals reported 44, 21, 5, 16, 29, 14, and 14 per cent for an average 17.6 per cent. One of the above

studies with an alcoholism incidence of 39 per cent contained a note that the actual incidence was 62 per cent when a history relative to alcohol was specifically recorded.

Another group, Thompson et al.,[48] studied 89 indigent patients presenting initially with acute pancreatitis and these workers were successful in following 76 survivors for periods of 1 to 7 years. Of these chronic alcoholics had a 72 per cent recurrence, non-alcoholics a 29 per cent recurrence, and a group with incomplete information as to alcoholism status suffered a 60 per cent recurrence of pancreatitis with the total for all of the groups being 57 per cent. The authors felt these indigent patients were at an added risk by reason of environmental factors which lead them to drink excessively and usher in the initial acute episode and would further tend to prevent adequate following of any therapeutic regimen, including abstinence from alcohol, and perhaps would contribute to an overall decreased resistence to any disease process.

With the above factors in mind, it is not difficult to accept nor surprising to find a wide variation in the incidence of pancreatitis associated with alcoholism. The current series is within the limits recorded in the literature and is found to be in the lower range, 8 per cent with the record low being 3.5 per cent.

Jaundice was present in the current series in a total of 36

per cent. Jaundice has not been recorded with regularity in the series of other authors, but Edmondson et al.[10] note 5 per cent occurrence and Comfort et al.[9] record the highest figure of 27.5 per cent. Of the 9 patients with jaundice 5 of these had a chronic pancreatitis associated with their acute pancreatitis, or 55.6 per cent. Another way of looking at it is that 83 per cent of the patients having both acute and chronic pancreatitis had an elevated bilirubin or were jaundiced, in the current series.

Cholelithiasis was present in 20 per cent and cholecystitis in 16 per cent of the current series. Hepatomegaly was recorded in 36 per cent. Surgical absence of the gallbladder occurred in 16 per cent and gallbladder distention in 12 per cent. Howard and Jordan[22] record their findings with regard to "gallstone pancreatitis" and those of others as follows:

TABLE VII

GALLSTONE PANCREATITIS

Author	Total Patients	Male No.	Male %	Female No.	Female %	Average Age
Howard & Jordan	168	45	27	123	73	53
Bockus et al.	36	16	44	20	56	50
Bell	100	45	45	55	55	59

The exact role of the liver and biliary system in the production of pancreatitis and the validity of Opie's "common channel theory" and bile reflux are still being investigated with contrasting evidence being obtained.[5, 20, 49, 51] However, it

seems difficult to deny some interaction between liver and pancreas in view of the work of Comfort et al.[9] where the patients were selected so as to supposedly eliminate those with biliary or gastrointestinal disease, but investigation showed these systems had the carefully ruled out pathology. Several other authors have noted an apparant clinical relationehip.[6, 10, 14, 22, 26, 31, 34, 44, 48]

Howard[22] states that a gallstone in the intrapancreatic portion of the common bile duct may be an etiologic factor in acute pancreatitis. He believes the presence of stones within the gallbladder is often associated with acute recurring pancreatitis and the course of this disease may be interrupted by cholecystectomy. He warns that surgery in the vicinity of the head of the pancreas may result in acute pancreatitis, especially choledochostomy and subtotal gastric resection. He lists as "fancies" bile reflux into the pancreatic duct and pancreatic duct obstruction being responsible for acute pancreatitis. He cites a personal series of 353 patients with acute pancreatitis in which he found 168 with cholelithiasis, an incidence of 48 per cent. In a collected series of 2,914 patients with acute pancreatitis he found 1,144 with cholelithiasis, or 39 per cent. Of his series of 168 patients with gallstones he found 28 with common duct stone an incidence of 16.6 per cent. He noted that 62 patients, 36.9 per cent, had recurrent attacks, occurring

chiefly before cholecystectomy.

Blumenthal and Probstein found biliary obstructive disease was present in 17 of their 163 patients, 10.4 per cent. The age range was 45 to 93 years. They cite other authors as finding ampullary stones in 4.4 per cent of over 1,200 cases of acute hemorrhagic pancreatitis and in 7.2 per cent of another 125 cases.

Joske[26] noted the presence of gallstones in 26 of his 90 patients, 28.9 per cent, and the absence in 42 cases. He obtained a history of gallstones in 14 patients, 15.6 per cent, and found no definite history available with regard to this condition in 8 patients or 8.9 per cent. Only two of the 26 patients with cholelithiasis had stones in the common bile duct and none of these had stones impacted at the ampulla of Vater. After removal of the stones, Joske found pancreatitis to be persistent in 14 patients in his series, or 53.8 per cent. He concluded his series did not show any evidence that bile reflux into the pancreatic ducts caused by gallstones had any etiological bearing upon pancreatitis.

Joske thought there was a clinical and definite pathological association between pancreatitis and cholelithiasis. His series showed 23 of the 90 patients, 25.6 per cent, had either a partial or complete obstruction of the common bile duct and he suggested this might result in cholelithiasis secondary to the pancreatitis. As a second possibility he mentions the evidence

supporting production of pancreatitis by hyperlipemia and suggests that hyperlipemia may have an etiologic relationship to both cholelithiasis and pancreatitis.

Comfort et al.[9] found 21.5 per cent of their patients, who had been picked so as to eliminate associated disease of the biliary and gastrointestinal tract, with a dilated and thin-walled gallbladder and an additional 7 per cent with gallbladder enlargement. They attributed these changes to the pancreatitis. Meyers and associates found cholecystitis in 31 per cent of their series and approximately half of these patients had cholelithiasis.[31] Blumenthal and Probstein compared autopsy patients having hepatic jaundice without pancreatitis and those with pancreatitis.[6] In a total of twenty-seven cases with choledocholithiasis, in which they felt the common channel theory might apply, they found only ten, or 37 per cent, with an acute pancreatitis. When they considered all types of obstructive disease of the common duct, a total of 95 cases, they found that only 16 patients, 16.8 per cent had developed acute pancreatitis. However, common duct obstruction, all types, was found in association with acute pancreatitis 4.4 times more often than duct obstruction without pancreatitis. They also found this association to be much higher in certain age and sex groups, i.e., females 71-80 years had an incidence of 66.7 per cent, males in the group 80-Plus had 33.3 per cent and females in this group had 33.3 per cent incidence. The validity of the significance is doubtful, as they readily

admit, in these older age groups because the number of patients is small.

Howard stresses the recurrent nature of gallstone pancreatitis and cites an earlier study of 40 patients with untreated cholelithiasis who were found to have a recurrence incidence of 53 per cent of pancreatitis during a one to seven year period of study, with a three year average.[22] He feels that while recurrence is frequent in pancreatitis associated with gallstones it seldom progresses to pancreatic insufficiency. Citing experience with 168 patients with gallstone pancreatites he found 6 per cent died in the initial attack, 62 patients or about 37 per cent suffered secondary attacks and of this group 3 to 5 per cent expired from their attacks. While the acute and recurrent attacks might be fulminating there was a tendency toward limitation of pancreatic fibrosis and its attendant sequelae and Howard sees fit to designate this as a "beneign course" for there were no deaths attributable to chronic pancreatic sequelae in this group of 168 patients. While not minimizing the danger to a patient during an acute attack, he points out that the natural history of the disease is toward a better tolerated chronic injury to the pancreas.

Cirrhosis of the liver was found in nine of the patients for a total of 36 per cent. Blumenthal and Probstein cite the findings of Pollack and Gerber* who stated that interstitial inflammation

*Pollack, A. D. and Gerber, I. E., Arch. Path., 36: 608, 1943.

of the pancreas is an almost universal finding in all forms of cirrhosis of the liver and noted a frequent occurrence in acute or subacute yellow atrophy. Pancreatic fat or parenchymatous necrosis does not appear to have been described in this association prior to their report where they found about 25 per cent of 88 patients with liver disease to have such pathology in Laennec's cirrhosis, acute and subacute yellow atrophy, toxic cirrhosis and cholangiolitic cirrhosis. When Blumenthal and Probstein excluded all other hepatic disease except cirrhosis they found cirrhotics without pancreatitis to be 4.4 per cent males and 6.0 per cent females. Patients with cirrhosis of the liver and acute pancreatitis were 11.7 per cent male and 10.1 per cent female. Howard states that the majority of patients with acute pancreatitis can be found to have either alcoholism or gallstones.[22]

Owens and Howard[34] compiled a collected series of cases totaling 333 patients, 32 of their own, in a study of pancreatic calcification as a late sequel in the natural history of chronic alcoholism and its relationship to pancreatitis. They found 63 cases of portal cirrhosis, approximately 19 per cent, but this included several patients who were noted only as having hepatomegaly.

One of the more comprehensive studies of cirrhosis and its association with pancreatic lesions is the review of 200 cases by

Steigman and Chung.[44] The cases were graded with respect to the degree of inflammation, fibrosis, and ectasia of acini versus the degree and activity of liver cirrhosis. They carefully define their criteria for grading on a one through four basis. They found with regard to pancreatic fibrosis and cirrhosis that 26 per cent of all cirrhotics had a grade 1 fibrosis, 45 per cent had a grade 2, 24 per cent had a grade 3, and that the extreme destruction of a grade 4 fibrosis was present in only 5 per cent of cirrhotics. In a comparison of cirrhotics with ascites against cirrhotics without ascites they found cirrhotics with ascites had 35 per cent of the group showing a marked fibrosis of the pancreas, a grade 3 or 4. Cirrhotics without ascites were found to have a marked fibrosis, of grade 3 and 4, of the pancreas in only 19 per cent. With regard to pancreatic inflammation they found 79 of the 200 cirrhotic patients without ascites had pancreatic inflammation or 39.5 per cent. Twenty-four of this group had fat necrosis, 12 per cent of the total. Among the cirrhotics with ascites they found 121 of the group showing inflammation of the pancreas, or 60.5 per cent. Of this group with ascites 27 patients, 13.5 per cent, had fat necrosis. They found cirrhosis with jaundice in 124 patients, 62 per cent. Cirrhosis without jaundice was found in 76 patients, 38 per cent. The authors concluded from their study of the 200 patients that there was a reciprocity of disease between the pancreas and liver in some patients.

The occurrence of gastrointestinal pathology in these patients with acute pancreatitis is covered by Table IV, pages 15 through 18. The first item under surgical procedures, "For Diseases of G-I Tract," in Table IV includes operations upon the liver and biliary system. The fact that some of these patients had more than one procedure under this category is not shown. Under the category of, "Abdominal Operations for Other Organ Systems," are the gynecologic procedures, nephrectomy, splenectomy, and others. It was found that 12 patients, or 48 per cent, had undergone surgery under the first item described above. Patients who had abdominal surgery for other than gastrointestinal disease amounted to 24 per cent of the total.

Howard states that surgical trauma around the region of the head of the pancreas can result in acute pancreatitis. He says that the biliary tract operations which resulted in pancreatitis have always included choledochostomy. Another operation which he strongly indites is the subtotal gastric resection. He believes these two operations account for most of the immediate postoperative acute pancreatitis seen.[22] He cites a study of 30 patients with various biliary tract procedures who were followed by serial tests of the serum amylase postoperatively. He found a significant amylase elevation in only 9 per cent following simple cholecystectomy. Significant elevation occurred in 29 per cent of those having operations which involved opening or explor-

ation of the common duct. He collected 88 cases of pancreatitis following biliary tract surgery, various authors from 1936 to 1958, in which there were 71 deaths, or 80.7 per cent. Of this group of 88 patients 79 had complete information regarding the operation and of the 79 it was found that 75 had a choledochotomy. There were 62 deaths from pancreatitis following cholodochotomy for a mortality rate of 83 per cent from this procedure. He also cites a study regarding the occurrence of acute pancreatitis following insertion of a long-arm T-tube. This study was again a collected series plus one of the authors patients. In this group of 17 patients who had a long-arm T-tube inserted into the common duct 16 expired due to pancreatitis, a fatality rate of 94 per cent. With regard to postgastrectomy pancreatitis Howard presents another collected series totaling 93 patients, 13 from his own experience, extending from 1934 to 1959. Of the 93 patients who had postgastrectomy pancreatitis 64 expired, or approximately 69 per cent. He believes that undoubtedly local factors account for the acute pancreatitis above and probably in cases of splenectomy and nephrectomy. However, he states such factors cannot account for pancreatitis which has been known to follow burns, neurosurgical operations, appendectomy, resection of parathyroid adenoma, prostatectomy, fractures, thyroidectomy, cecostomy, sigmoid colostomy, cesarean section, herniorrhaphy, and femoral embolectomy. He suggests that the occurrence of

pancreatitis after anatomically unrelated trauma might be related to vagal stimulation by an unknown hypothalamic mechanism. He also suggests the possibility of drug induced spasm of the sphincter of Oddi being responsible for postoperative pancreatitis and this view is supported by the work of other authors.[3, 24, 33, 42]

Of the patients in this series four, or 16 per cent, had a history of biliary tract surgery and two with recent surgery. One of these, a 64 year old woman, had a subtotal gastrectomy with gastrojejunostomy following an episode of hemorrhage two and one-half years prior to her final admission. She entered the hospital after being in a hospital in another part of the state for ten days, where she had been told she had hepatitis. She had a history of painless jaundice of less than one month, recently progressively worse, stools becoming lighter and urine darker. Following symptomatic treatment and diagnostic workup she was taken to surgery, as indicated, and cholecystectomy, cholodochostomy, duodenostomy, and liver biopsy were performed. The pathology report indicated chronic cholecystitis, diverticulosis of the gallbladder, cholelithiasis, ascending cholangitis of the liver and cicatrix of the anterior abdominal wall. The patient did well for several days postoperatively, but apparantly began an ingravescent course on the seventh postoperative day. The white blood cell count rose to 54,100 per $mm.^3$ with marked left shift and toxic granulation of cells. The serum amylase and lipase were within normal limits. The white blood cell count rose to

85,000 per mm.^{3} with continued left shift on the ninth post-operative day and a fetor hepaticus was noted. A grade II apical heart murmur was present. Although vigorous therapeutic measures were continued the patient followed a progressive downhill course and expired on her eleventh post-operative day. The autopsy revealed biliary cirrhosis, an ascending cholangitis, areas of necrosis and subacute and chronic inflammation of the pancreas, and an early bronchopneumonia in the lower lobe of the right lung.

The other patient with recent biliary tract surgery was a 67 year old male who had been hospitalized at an Air Force Base Hospital in California. Features of his illness there had been jaundice, dysuria, dark urine, marked malaise and weakness, and a proteus bacteremia. A laparotomy was performed with cholecystectomy, choledochostomy, and a liver biopsy which was interpreted as post-necrotic cirrhosis. A well-functioning T-tube was left in place. His postoperative course was progressively downhill with increasing jaundice, lethargy, and generalized malaise and weakness. After admission to this hospital he continued to become increasingly jaundiced, there was progressive oliguria, acidosis, and azotemia, with hypoalbuminemia and hyponatremia noted. Physical examination revealed a very ill, jaundiced, white male with a blood pressure of 74/48 mm. Hg., questionable spider nevi, a systolic heart

murmur, abdominal distention, and a questionably ballotable hepatomegaly. During his hospital course, which was progressively downhill, he had increasing electrolyte imbalance and a rising blood urea nitrogen, to as high as 143 mg./100 ml. On his last day a hemodialysis was performed in an attempt to restore normal electrolyte balance, but during the procedure he had a sudden emesis of approximately 1,500 cc. of pure blood and expired. Autopsy revealed death to be due to massive gastrointestinal hemorrhage from ruptured esophageal varices. He had a marked post-necrotic type of cirrhosis, an acute pancreatitis with areas of focal necrosis, and also an acute tubular necrosis. He expired approximately 6-7 weeks postoperative.

Four patients had subtotal gastrectomies, three with a gastrojejunostomy. One of the gastrojejunostomy patients, a 64 year old female, had done well for two and one-half years and her final hospital course following biliary surgery is described on pages 31 and 32. The other two gastrojejunostomy patients died 12 days postoperative, a 60 year old male, and 17 days postoperative, a 62 year old male. The cause of death in the 60 year old male a pulmonary embolus arising either from the pancreas or lower extremeties. The cause of death in the 62 year old male was overwhelming infection and inanition with contributing factors being fatty metamorphosis of the liver, ascending cholangitis, and early biliary cirrhosis. The fourth patient with a subtotal

gastrectomy had this procedure in conjunction with an esophagectomy. He did poorly immediately after surgery with persistent hypotension, tachycardia, and abdominal distention. He was returned to the operating room the same day where a laparotomy with splenectomy was performed because of bleeding in the splenic fossa. The following day he complained of lower thoracic and upper epigastric pain of severe nature with radiation posteriorly into the back. An electrocardiogram showed wandering pacemaker, left interventricular block, probable left ventricular hypertrophy, and a probable myocardial ischemia. The patient continued to do poorly and on the eighth postoperative day evisceration occurred. He was taken to the operating room where the wound was closed, but he expired quite suddenly later that day. The immediate cause of his death appeared to be related to the trauma of evisceration and subsequent closure of the wound.

Stomach ulcers were found in two patients, 8 per cent, and duodenal ulcers in two patients, one with penetration into the pancreas. Stomach hemorrhage was recorded in 24 per cent. A history of melena was recorded in four patients, 16 per cent, two of these having hematemesis recorded. Comfort et al.[9] state that gastrointestinal involvement is common, noting both decreased and increased motility and hemorrhages, but did not give the incidence of their occurrence. Howard[22] records delayed gastrointestinal hemorrhage as the cause of death in 32 per cent

of a series of 44 patients. Massive hemorrhage occurred, most characteristically through drainage tracts, but also as melena and hematemesis. Hemorrhage appeared between the second and fourth weeks postoperatively. He cites three cases in which there appeared to be first a necrosis of the pancreas followed by infection then massive hemorrhage and death. One of these cases had a prophylactic delayed debridement and drainage of the necrotic, infected pancreas and subsequently recovered.

Howard lists gastrointestinal hemorrhage source in 15 patients as 11 with bleeding from major intraperitoneal veins, i.e., vena cava, portal vein, and mesenterics, for an incidence of 73.4 per cent. Eight with multiple superficial erosions of the gastrointestinal tract, or approximately 53 per cent. Citing the experience of two other authors, one with a total of 10 patients, the hemorrhage source was unspecified in most, but was a gastric ulcer in one patient and duodenal ulcer in another. The other series had 5 patients, 3 with duodenal ulcer hemorrhage, 1 with hemorrhagic duodenitis, and 1 with acute superficial gastric ulcers.

Meyers et al.[31] lists gastrointestinal hemorrhage as a complication in 5 per cent. They suggest hemorrhage may be due to deficient coagulability of the blood, based on the work of other investigators. Blumenthal and Probstein list gastrointestinal hemorrhage as occurring in 12 per cent, but do not list melena or hematemesis. However, they cite others as finding melema

in 4.5 per cent and hematemesis in 3.1 per cent. Thus, the findings of the current series are at variance with these authors by a factor of 2 to 4.8 with regard to gastrointestinal hemorrhage and 2.58 in hematemesis and 3.56 in the case of melena.

SUMMARY

A study of 25 patients with the diagnosis of acute pancreatitis on their autopsy record has been made in order to determine and correlate any association or reciprocity between diseases of the biliary tract and the gastrointestinal system with acute pancreatitis. The existence of such a relationship is strongly supported by the works of Comfort et. al.[9] and that of Steigman and Chung.[44] Upon careful review, several other authors tend to support this relationship, directly or indirectly.[6, 9, 11, 14, 22, 26, 27, 47, 49, 51]

There were 13 females and 12 males in this series, ranging in age from 40 to 88 years. There were 5 deaths in which the pancreatitis played the major role, 2 females and 3 males, and may have been responsible in one other case. The causes of death in these patients were, (1) female age 44, intractible shock secondary to acute necrotizing pancreatitis, (2) female age 49, acute and chronic pancreatitis with fat necrosis amd digestion of part of duodenum and jejunum with abscess formation, in addition there was marked biliary cirrhosis and cholemic nephrosis, (3) male age 60, pulmonary embolism arising from area of acute pancreatitis or the lower extremeties, (4) male age 62, severe hemorrhagic pancreatitis and bleeding from stress ulcers, and, (5) a male age 65, peripheral vascular collapse secondary to acute hemorrhagic pancreatitis. Of the 25 patients, evidence of a

chronic pancreatitis was found in 6 patients.

Age and sex distribution in patients with acute pancreatitis in the current series is compared with a similar series of 163 autopsy patients studied by Blumenthal and Probstein. While it is realized comparison of a small group of 25 patients with a larger group of 163, approximately 6.5 times larger, offers difficulties it seems safe to say there are differences in the two populations. Areas of notable difference are the 41-50, 61-70, and the 81 Plus age groups. These are readily seen in Table V, page 19. Information concerning age and sex distribution, with regard to the current series only, can be found in Table I, page 7.

Pathology of the liver and biliary system are detailed in the Table II, pages 8 and 9. Fatty metamorphosis was found in 32 per cent, liver congestion in 76 per cent, ascites in 40 per cent, cholangitis in 12 per cent, cholalithiasis in 20 per cent, cholacystitis in 16 per cent, hepatitis in 8 per cent, jaundice in 36 per cent, carcinoma metastatic to the liver in 8 per cent, hepatomegaly in 36 per cent, cirrhosis of the liver (all types) in 36 per cent, and a history of alcoholism in 8 per cent. There was one case with thrombotic thrombocytopenic purpura which involved not only the liver, but many other organs as well. Discussion and comparison with the literature regarding the above factors in Table II and the role of biliary tract surgery in the production of pancreatitis has been done.

The pathologic conditions found in the pancreas of the patients in the current series are given in Table III, page 13. In addition to the acute pancreatitis common to all of these patients, there was chronic pancreatitis in 24 per cent, fat infiltration of the pancreas in 40 per cent, fat necrosis in 44 per cent, fibrosis in 28 per cent, calcium deposits in the pancreas in 20 per cent, edema of the pancreas in 28 per cent, and islet cell changes in 24 per cent. Diabetes mellitus was present by history in 8 per cent, two patients, one having islet cell changes recorded with no changes in the other. Two other patients had hyperglycemia recorded during their hospital course with islet cell changes in both. However, neither had a known history of diabetes mellitus and there was a question whether or not the hyperglycemia was due to previously undiagnosed diabetes or resulted from the acute pancreatitis, as reported in the literature.[6, 14, 22, 27, 44, 47]

Pathologic conditions of the gastrointestinal tract are recorded in Table IV, pages 15 through 18. Surgical procedures for disease of the gastrointestinal tract had been performed in 48 per cent and abdominal surgery in connection with other organs was found in 24 per cent. The role of abdominal and other surgical procedures as described in the literature is set forth. The vital role of biliary tract procedures and subtotal gastrectomy and gastrojejunostomy operations in the production of acute postoperative pancreatitis with an attendant high mortality rate seems

quite evident and may have been a factor in some of the patients in the current series.

Esophageal varices were present in 12 per cent, esophageal perforation in 8 per cent. Esophagitis was present in 8 per cent. One patient had had a recent esophagectomy for epidermoid carcinoma of the esophagus.

Some of the disease conditions found in the stomach were, ulcers in 8 per cent, hemorrhage in 24 per cent, gastroenteritis in 8 per cent, and the following named were found in one patient each, or 4 per cent, chronic gastritis, polypoid adenocarcinoma, leiomyoma, infarct, and partial obstruction.

Lesions found in the small intestine were, focal ulceration of the pylorus in 4 per cent, an ulcer of the duodenum penetrating into the pancreas in 4 per cent, pancreatic enzyme necrosis of duodenum and jejunum in 4 per cent, a hamartoma from the pancreas was found in the wall of the ileum in 4 per cent, one patient had an ileostomy, and one patient suffered an ileal infarct thought to be due to volvulus when she was in her third postoperative week following a jejunostomy.

Some of the findings related to the colon were diverticulosis in 12 per cent, colostomy in 4 per cent, surgical absence of the appendix in 20 per cent, recurrent carcinoma in the colostomy site in 4 per cent, adenocarcinoma of the rectum in 4 per cent, submucosal hemorrhage in 4 per cent, and a fibro-

purulent colitis. Melena was noted in 16 per cent and hematemesis in half of these, or 8 per cent. Peritonitis was found in 16 per cent of the patients.

CONCLUSIONS

1. There seems little doubt that alcoholism is an etiological factor in the production of both acute and chronic pancreatitis. While there is a variance in the incidence of alcoholic pancreatitis in the literature, there seems to be uniform acceptance of the ability of alcohol to produce the disease pancreatitis. Only the etiologic mechanism of alcohol and the true incidence of its production of pancreatitis seem in doubt. The current series had an alcoholic history recorded in 8 per cent, two patients, one of these, a 40 year old female, apparantly died due to alcoholism and had a slight acute hemorrhagic pancreatitis, but only liver congestion and an acute slight hepatitis. The other patient, a 47 year old female, had acute and chronic pancreatitis with marked changes in the pancreas as well as Laennec's cirrhosis. There seems little doubt but what alcohol may have played a major role in these two patients. The incidence of alcoholism associated with pancreatitis in the current series fell within the lower end of the range reported in the literature, from 3.5 to 60 per cent or more.

2. The variation of alcohol as an etiologic mechanism in the production of pancreatitis, both acute and chronic, as seen in the literature is probably due to inherent differences in the patient populations, i.e., groups of indigent patients compared with private patients, or higher income groups. Regional vari-

ations and group customs, religious and national background, as well as racial factors should be considered in comparisons made with collected series. Comparison of groups with regard to these factors is usually possible to only a limited extent.

3. Diabetes mellitus is known to be a complication of pancreatitis, one author reporting 13.5 per cent in acute pancreatitis[6] and another 11 per cent in chronic pancreatitis with calcification.[22] Hyperglycemia occurring during an acute attack has also been noted, an opinion cited by one group[47] is about 10 per cent. The current series had two patients, 8 per cent, with a known history of diabetes, one of which had moderate hyalinization of the islet cells and the other no changes in the islet cells. An additional two patients, 8 per cent, evidenced hyperglycemia during their acute attack, both showing islet cell changes (one cell necrosis and the other cell enlargement and granularity), and there was a question whether the patients were previously undiagnosed diabetics or if the hyperglycemia stemmed from the effect of the acute pancreatitis upon the islet cells. The findings in the current series with regard to diabetes mellitus and hyperglycemia during an acute attack of pancreatitis seem to be consistent with that reported in the literature.

4. Cholecystitis and cholelithiasis seem to contribute to the occurrence of pancreatitis and the entity "gallstone pancreatitis" as described by at least one group[22] appears to be one which is valid. Cholecystitis and cholelithiasis occurred in

combination in 12 per cent of the current series. An additional 16 per cent had cholelithiasis recorded at autopsy. Another 12 per cent had a history of cholecystectomy at some time in the past. Another patient belonging to the group having both cholelithiasis and cholecystitis was 11 days post-cholecystectomy at the time of her death. One patient in the group of 12 per cent with a history of cholecystectomy was in his 6-7th post-operative week at the time of death. Another patient was in his 13th post-operative day following cholecystostomy and removal of gallstones when he expired.

5. Operative procedures may cause pancreatitis, most likely due to trauma, and among the worst offenders are biliary surgery combined with choledochostomy and subtotal gastrectomy with a gastrojejunostomy. When pancreatitis results from the above procedures it is quite likely to be very severe and results in a fatal outcome in the majority of patients.

6. Pancreatitis may occur in conjunction with operative procedures far removed from the immediate region of the pancreas and while the mechanism in the production of pancreatitis is not always clear it seems likely that some of the drugs given to the patient during the post-operative period may be responsible.

7. The reciprocity between cirrhosis and changes in the pancreas, as reported by Steigman and Chung[44] and as found by Comfort et al.,[9] seems to be supported by the findings in the current series of patients.

8. There seems to be an association or reciprocity between disease states of the gastrointestinal tract and pancreatitis in some patients.

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